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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,354	HARIRI ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 25-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 25-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/27/05; 2/16/05;6/18/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-13 and 25-36 are all the pending claims for this application.

2. The preliminary amendment of the specification filed 6/18/07 has been considered and entered.

Election/Restrictions

3. Applicant's election without traverse of the species for hydrocortisone (stem cell culture conditions), HTB-104 (tumor cells), and acid fibroblast growth factor (aFGF; stimulator of angiogenesis) in the Reply 9/21/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The species of stem cell culture condition for EGF (Claim 5) is rejoined for examination.

The species of angiogenesis stimulator for angiogenin, bFGF, EGF, IL-8, PGF, PDGF, HGF, TGF-alpha, TNF-alpha, VEGF and PGE2 (Claim 36) are rejoined for examination.

4. Claims 1-13 and 25-36 are all the pending claims under examination.

Priority

5. Applicants priority claim to U.S. Provisional Application No. 60/372, 127 (filed 4/12/02) is acknowledged, however, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/372,127, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application.

Claim 1 is drawn to culturing the stem cell in the presence of the test compound where in Claim 5, hydrocortisone is additionally added. Provisional application '127 does not describe the additional step of growing the stem cells in hydrocortisone (or the non-elected species for bovine brain extract).

Claim 1 is drawn to culturing the stem cells in the presence of the test compound where tumor cells are additionally added (Claim 3) and the tumor cells are cell lines (Claim 4) which include HTB-104 cells (Claim 31). Provisional application '127 does not describe the additional step of growing the stem cells in the presence of tumor cells much less the HTB-104 cell line (or the non-elected species for tumor cells).

Claim 13 is drawn to culturing a vessel section with tumor cells in the presence of the test compound where the tumor cells are HTB-104 (Claim 32). Provisional application '127 does not describe the additional step of growing the vessel in the presence of tumor cells much less the HTB-104 cell line (or the non-elected species for tumor cells).

Claims 1, 2, 6-12, 25-30, 33-36 obtain benefit of the provisional application filing date of 4/12/2002.

Claims 3-5, 13, 31 and 32 obtain benefit as of the 317 application, PCT/ US03/11578 filing date of 4/14/2003.

Should Applicants wish to obtain benefit of the provisional application filing date for Claims 3-5, 13, 31 and 32, they are invited to identify the supporting disclosure by page and line number.

Information Disclosure Statement

6. The U.S., international and foreign patent references and the non-patent literature references cited in the IDS' of 1/27/05, 2/16/05, 6/18/07 and 10/4/07 have been considered and entered.

Specification

7. The disclosure is objected to because of the following informalities:

a) The cross-reference to the priority documents fails to include the 371 application, PCT/US03/11578, filed 4/14/03.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-13 and 25-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claims 1-12, 31 and 33-36 are indefinite for the recitation "a plurality of stem cells" in Claim 1 because the meaning of the phrase is not defined by the claim. Does the term "plurality" mean a certain number of a homogenous population of stem cells or any number of stem cells so long as the stem cells are heterogeneous or a pluripotent stem cell? Further, the claim does not define the phenotype of the stem cell or the origin of the stem cell, for example, if the stem cell is human embryonic-derived, bone-marrow derived, mesenchymal, etc. Could any stem cell of any phenotype be induced to differentiate into a microvessel under the culture conditions?

b) Claims 1-13 and 25-33 recite the limitation "said control level" in line 8 of Claim 1 and line 9 of Claim 13. There is insufficient antecedent basis for this limitation in the claims. Claims 1 and 13 recite "a control amount of microvessel outgrowth."

c) Claims 1-13 and 25-36 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the steps describing

the relationship or correlation between the endothelial growth and the microvessel outgrowth from the stem cells in Claim 1 and the microvessel outgrowth from the vessel section in Claim 13. It is not apparent if the endothelial outgrowth is a function of microvessel outgrowth, or an independent parameter of the screening method. Further, claims 1 and 13 recite "for a time and under conditions in which endothelial cells grow" and it is not clear if the culture conditions for treating the stem cells (Claim 1) or vessel section (Claim 13) should be the same as those permissive for endothelial cell growth irrespective of whether endothelial cells are actually grown in the method assay. One of skill cannot discern the direct if any relationship between the growth of endothelial cells and the induction of microvessel outgrowth in the presence of the test compound in view of the limitation that the conditions are "for a time and under conditions" for endothelial cell growth. Is endothelial cell growth critical or required for microvessel outgrowth to occur and for determining a test compound for angiogenesis modulation?

d) Claim 3 is indefinite for the recitation "a plurality of tumor cells" because the meaning of the phrase is not defined by the claim. See the Examiner's comments above for the term "plurality" as they would relate the intended tumor cell populations.

e) Claim 36 recites the limitation "said stimulator of angiogenesis". There is insufficient antecedent basis for this limitation in the claim or in Claim 34 from which the claim depends.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

9. Claims 1-9, 12, 13, 29, 30, and 34-36 are rejected under 35 U.S.C. 102(e) as being anticipated by Drake et al. (WO 01/63281; published 8/30/01; priority to 2/23/00; cited in the IDS of 10/4/07).

Claims 1-9, 12, 29, 30, and 34-36 are interpreted as being drawn a method of identifying a modulator of angiogenesis or vasogenesis comprising culturing a plurality of stem cells with a test compound under conditions for endothelial cell growth and comparing endothelial-microvessel outgrowth between the test sample and a control sample (Claim 1), where the stem cells are cultured with a vessel section (Claim 2), the cultures contain a plurality of tumor cells (Claim 3), and the tumor cell is a cell line (Claim 4), the stem cells are cultured in EGF (Claim 5), the agent is an anti-angiogenic

agent (Claim 6) or an angiogenic agent (Claim 7), and culturing the stem cells for at least 7 days (Claim 8) or 14 days (Claim 9), the stem cells are cultured in a gel comprising a non-denatured collagen (Claim 12), the stem cells are bone-marrow derived (Claim 29) or mesenchymal (Claim 30), and the control microvessel outgrowth is measured in the absence (Claim 34) or presence of an angiogenesis stimulator (Claim 35), and the angiogenesis stimulator is VEGF, bFGF, or HGF (Claim 36).

Claim 13 is interpreted as being drawn to a method for identifying a modulator of angiogenesis comprising culturing a vessel section in the presence of a plurality of tumor cells and a test compound under conditions that enable the growth of endothelial cells and tumor cells and comparing microvessel outgrowth from the vessel between the test and a control sample.

Drake discloses a method for screening an agent (agonist or antagonist) that promotes or inhibits angiogenesis or vasculogenesis comprising culturing embryonic, allantoic or mesodermal (mesenchymal) stem cells with the agent, and detecting an increase in endothelial cells in the culture compared to a control culture, where the increase indicates that the agent promotes vasculogenesis and a decrease in endothelial cells indicates an agent that inhibits vasculogenesis (pp. 3, line 13- p. 4, line 6). Drake teaches that allantoic cells or an ex vivo culture of allantois that includes mesodermal stem cells (mesenchymal) and endothelial cells can be used to screen for factors that affect angiogenesis and/or vasculogenesis (p. 3, line 7-9). Drake discloses that the method also allows for the detection of the formation of vasculature or vascular remodeling (p. 4, lines 22-23) such as the formation of vascular networks (p. 10, lines

20-21). Drake teaches that the method substrate can include bone-marrow derived stem cells or allantois, explant, organ, tissue, graft or tumor, and adding the test agent to the culture medium (p. 12, lines 28-29). Drake teaches de novo vessel formation by vasculogenesis are overlooked using screening methods with only endothelial cells because endothelial cells can only be used to measure angiogenesis where allantoic mesodermal stem cells allows observation of vasculogenesis (p. 8, line 24-29). Drake teaches that the agent and cells should "be cultured for 1-48 hours, but the time can vary depending on the half life of the agent and could be optimized by one skilled in the art using routine experimentation" (p. 13, line 6-10) or culturing in medium "for weeks or months" (p. 12, line 23). Drake discloses that an agent that promotes or inhibits vasculogenesis or angiogenesis would be an agent that would also slow or prevent tumor growth (p. 15, lines 11-22). Drake teaches a GelFoam sponge assay composed of collagen type I (p. 37, line 34- p. 38, line 5) for growing endothelial stem precursors and soaking the sponges in the angiogenesis stimulator, VEGF (Example 9) or treating allantois with VEGF, bFGF and HGF (Example 5). Drake teaches assays using human breast carcinoma cell lines (Example 10).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 1 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drake et al. (WO 01/63281; published 8/30/01; priority to 2/23/00; cited in the IDS of 10/4/07) in view of Fox et al. (J. Pathol. 179:232-237 (1996); cited in the IDS of 1/27/05).

The interpretation of Claims 1 and 36 is discussed supra. Claim 36 is further drawn to the angiogenesis stimulator being aFGF, angiogenin, bFGF, EGF, IL-8, PGF, PDGF, HGF, TGF-alpha, TNF-alpha, VEGF and PGE2.

The claimed method of identifying a modulator of angiogenesis using stem cells was prima facie obvious at the time of the invention over Drake and Fox.

The interpretation of Drake is discussed supra. Drake teaches culturing the stem cells in culture medium and the addition of the angiogenesis stimulators aFGF, angiogenin, bFGF, EGF, IL-8, PGF, PDGF, HGF, TGF-alpha, TNF-alpha, VEGF and PGE2 to the culture, which Fox teaches as being essential to endothelial-associated microvessel outgrowth.

Fox discloses that endothelial cells produce sprouts from parent venules and angiogenic factors like aFGF, angiogenin, bFGF, EGF, IL-8, PGF, PDGF, HGF, TGF-alpha, TNF-alpha, VEGF and PGE2 (Table 1; p. 233, Col. 2, ¶3) which alter endothelial cell morphology (p. 233, Col. 1, ¶2), proliferation (p. 233, Col. 2, ¶6 to p. 234, Col.1) and microvessel differentiation (p. 234, Col. 1).

One skilled in the art would have been motivated and reasonably assured of success in having produced the method for identifying a modulator of angiogenesis using stem cells based on the combined disclosures of Drake and Fox. Drake discloses the culture conditions for assaying angiogenesis modulators (agonist and antagonist) which effect stem cell differentiation into endothelial cells and the angiogenic mediators for formation of microvasculature. One skilled in the art could have readily modified the culture conditions of Drake by adding one or more or a combination of the angiogenic stimulators disclosed in Fox because Fox discloses that endothelial cells are responsive to the stimulators by proliferating and differentiation into microvessels. One skilled in the art would have been reasonably assured of success in having introduced the stimulators into the culture assay system of Drake because the stimulators were

recognized as being endogenous factors known to be essential for the proliferation and differentiation steps of endothelial cells into microvessels.

11. Claims 1, 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drake et al. (WO 01/63281; published 8/30/01; priority to 2/23/00; cited in the IDS of 10/4/07) as applied to claim 1 above, and further in view of Montesano et al. (J. Cell. Physiol. 132(3): 509-516 (1987); cited in the IDS of 1/27/05).

The interpretation of Claim 1 is discussed supra. Claims 10 and 11 are interpreted as being drawn to the stem cells being cultured on a fibrin matrix (Claim 10) or a physiological gel comprising fibrin (Claim 11).

The claimed method was prima facie obvious over Drake and Montasano.

The interpretation of Drake is discussed supra. Drake discloses using foamgels as supports for endothelial cell invasion and organization into vessel like structures, but does not disclose a fibrin matrix as does Montasano.

Montasano discloses the ability of endothelial cells to invade and organize into vessel-like structures using a fibrin matrix or gel (p. 509, Col. 2, ¶1), where endothelial cell cords extend downward into the fibrin matrix from the surface monolayer of cells.

One skilled in the art would have been motivated and reasonably assured of success in having produced the method for identifying a modulator of angiogenesis using stem cells based on the combined disclosures of Drake and Montesano. Drake discloses the culture conditions for assaying angiogenesis modulators (agonist and antagonist) which effect stem cell differentiation into endothelial cells and the formation

of microvessels using solid supports such as a foamgel. One skilled in the art could have readily modified the culture conditions of Drake by adding a fibrin matrix or gell disclosed in Montasano because Montasano discloses that endothelial cells are responsive to the stimulators by proliferating and differentiating into microvessels when grown on fibrin matrices or fibrin gels. One skilled in the art would have been reasonably assured of success in having introduced the fibrin matrix or fibrin gel into the culture assay system of Drake because the gels were recognized as providing a replica environment for the differentiation steps of endothelial cells into microvessels.

12. Claims 1 and 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drake et al. (WO 01/63281; published 8/30/01; priority to 2/23/00; cited in the IDS of 10/4/07) as applied to claim 1 above, and further in view of Zygmunt (Early Pregnancy 5(1):72-73 (Jan 2001)).

The interpretation of Claim 1 is discussed supra. Claims 25-28 are drawn to the stem cells being isolated from human placenta (Claim 25) where the placental stem cells are CD34- (Claim 26), or the placental stem cells are Oct-4+, SSEA3- and SSEA4- (Claim 27) or the placental stem cells are CD10+, CD29+, CD44+, Cd54+, CD90+, SH2+, SH3+ SH4+, OCT4+, CD34-, CD38-, CD45-, SSEA3- and SSEA4- (Claim 28).

The claimed method was prima facie obvious over Drake and Zygmunt.

The interpretation of Drake is discussed supra. Drake discloses using allantoic explants in assaying for stem cell differentiation into endothelial cell precursors for

formation of vessels structures and various other organs but does not disclose using placental-derived stem cells as endothelial cell precursors, which does Zygmunt.

Zygmunt discloses that placental vascularization occurs by vasculogenesis and angiogenesis and is mediated by endothelial progenitor cells present in the developing primitive organ. Zygmunt does not describe the phenotype of the placental stem cells for endothelial progenitors, but one of skill in the art would envisage that the endogenous placental stem cells inherently possess the phenotype of CD34- (Claim 26), or Oct-4+, SSEA3- and SSEA4- (Claim 27) or CD10+, CD29+, CD44+, Cd54+, CD90+, SH2+, SH3+ SH4+, OCT4+, CD34-, CD38-, CD45-, SSEA3- and SSEA4- (Claim 28), where the markers were already known in the art and the technology (PCR primers for detecting the respective mRNA or antibodies specific for each cell marker for FACS sorting) for separating cells with the phenotype was well within the ordinary skill of the artisan at the time of the invention. ("The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property, which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1997)).

One skilled in the art would have been motivated and reasonably assured of success in having produced the method for identifying a modulator of angiogenesis using placental-derived stem cells comprising endothelial progenitors based on the

combined disclosures of Drake and Zygmunt. Drake discloses the culture conditions for assaying angiogenesis modulators (agonist and antagonist) which effect allantoic-derived stem cell differentiation into endothelial cells and Zygmunt discloses that placenta also contains endothelial progenitor stem cells critical for forming blood vessels. One skilled in the art could have readily modified the culture conditions of Drake by introducing the placental-derived stem cells disclosed in Zygmunt and having the inherent phenotype and/or selecting for a phenotype of CD34-, *or* Oct-4+, SSEA3- and SSEA4-, *or* CD10+, CD29+, CD44+, Cd54+, CD90+, SH2+, SH3+ SH4+, OCT4+, CD34-, CD38-, CD45-, SSEA3- and SSEA4- because Zygmunt discloses that the placenta is rich in endothelial cell progenitors capable of forming vessel beds. One skilled in the art would have been reasonably assured of success in having introduced the placental-derived stem cells into the culture assay system of Drake because the stem cells were recognized as being endogenous cells known to be essential for differentiation into microvessels.

13. Claims 1 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drake et al. (WO 01/63281; published 8/30/01; priority to 2/23/00; cited in the IDS of 10/4/07) as applied to claim 1 above, and further in view of Crouse et al. (Kroc Found. Ser. 18:211-231 (1984)).

The interpretation of Claims 1 and 5 is discussed supra. Claim 5 is interpreted as further being drawn to the culture conditions where the stem cells are cultured in hydrocortisone.

The claimed method was prima facie obvious over Drake and Crouse.

The interpretation of Drake is discussed supra. Drake discloses assaying for stem cell differentiation into endothelial cell precursors for formation of vessels structures and adding culture supplements such as EGF but does not disclose adding hydrocortisone as does Crouse.

Crouse discloses that hydrocortisone is essential to maintaining primitive stem cells in vitro.

One skilled in the art would have been motivated and reasonably assured of success in having produced the method for identifying a modulator of angiogenesis using hydrocortisone in the culture medium to promote and maintained viability of primitive stem cells based on the combined disclosures of Drake and Crouse. Drake discloses the culture conditions for assaying angiogenesis modulators (agonist and antagonist) using stem cell-derived endothelial cells where EGF is added to the culture conditions and Crouse discloses that hydrocortisone is critical for maintaining bone-marrow-derived endothelial progenitor stem cells critical for forming blood vessels in the assay. One skilled in the art could have readily modified the culture conditions of Drake by introducing the hydrocortisone disclosed in Crouse because Crouse discloses the criticality in maintaining the viability and pluripotency of stem cells in vitro and one skilled in the art would have been motivated to have kept the stem cells in culture for the weeks required to assay the test agent effects on vessel formation. One skilled in the art would have been reasonably assured of success in having introduced the

hydrocortisone into the culture assay system of Drake because the hydrocortisone was recognized as being essential for long-term maintenance of primitive stem cells in vitro.

14. Claims 1, 2 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drake et al. (WO 01/63281; published 8/30/01; priority to 2/23/00; cited in the IDS of 10/4/07) as applied to claims 1 and 2 above, and further in view of Merrick et al. (Transplantation 62(8): 1085-1089 (1996)).

The interpretation of Claims 1 and 2 is discussed supra. Claim 33 is interpreted as being drawn to a vessel section of Claim 2 being an umbilical cord vessel cross-section.

The claimed method was prima facie obvious over Drake and Merrick.

The interpretation of Drake is discussed supra. Drake discloses assaying for stem cell differentiation into endothelial cell precursors for formation of vessels structures using mesodermal and allantoic explants but does not disclose umbilical cord sections as does Merrick.

Merrick discloses that human umbilical vein and artery were used to measure the presence of endothelial cells.

One skilled in the art would have been motivated and reasonably assured of success in having produced the method for identifying a modulator of angiogenesis using umbilical cord tissues as explants and a source of stem cells based on the combined disclosures of Drake and Merrick. Drake discloses the culture conditions for assaying angiogenesis modulators (agonist and antagonist) using allantoic stem cell-

derived endothelial cells and Merrick discloses human umbilical tissues as a source of observing endothelial cell proliferation. One skilled in the art could have readily modified the culture conditions of Drake by introducing the umbilical tissues disclosed in Merrick because the tissues were a source of endothelial cells. One skilled in the art would have been reasonably assured of success in having introduced the umbilical tissues into the culture assay system of Drake because the tissues were was recognized as being a source of endothelial cells in microvessels.

Conclusion

15. No claims are allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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